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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,267	11/30/2001	Isabelle Ahrens-Fath	SCH-1793	2581

23599 7590 10/19/2005

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EXAMINER	
PAK, MICHAEL D	
ART UNIT	**PAPER NUMBER**
1646	

DATE MAILED: 10/19/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/997,267	AHRENS-FATH ET AL.	
	Examiner	Art Unit	
	Michael Pak	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *4-11 and 16-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 12-15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *3-18-05; 5-21-02*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's election with traverse of Group I in the reply filed on 26 July 2005 is acknowledged. The traversal is on the ground(s) that the SEQ ID NO: 3 and 4 were not mentioned. This is found persuasive and nucleic acid of SEQ ID NO:1 and 3 are examined.

The requirement is still deemed proper and is therefore made FINAL.

Claim Objections

2. Claims 1-3 are objected to because of the following informalities: claim recites "Seq ID NO 1 and/ or 3" which contains a mispelling. The correct spelling is suggested such as "SEQ ID NO:1" or "SEQ ID NO:3." Appropriate correction is required.

3. Claim 1 is objected to because of the following informalities. Claims contain multiple periods for punctuation and only one is allowed and required.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

4. Claims 1-3, 12-13 and 15 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims, as written, do not sufficiently distinguish over cells that exist naturally because the claims do not particularly point out any non-naturally occurring differences

between the claimed products and the naturally occurring products. In the absence of the hand of man, the naturally occurring products are considered non-statutory subject matter. *See Diamond v. Chakrabarty*, 447 U.S. 303, 206 USPQ 193 (1980). The claims should be amended to indicate the hand of the inventor, e.g., by insertion of "Isolated" or "Purified" as taught by page [insert page number] of specification. See MPEP 2105.

Claims are drawn to product of nature or method using product of nature because the claims do not include terms which show that a "hand of man" was involved in the claimed product.

5. Claim 15 is rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claim 15 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim 15 is a "use claim" which is not a proper process claim. MPEP 2173.05(p).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the

art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1-3 and 12-15 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recite "androgen receptor" in line 1 which is confusing because AR42 and AR32 do not have transactivating activity with androgen and thus is not an androgen receptor (see specification page 18).

Claim 1 line 2 recite "characterized in that it" which is indefinite because it is an indefinite pronoun and it is not clear what "it" is referring to. Furthermore, it is not clear what is the metes and bounds of the term "characterized in that" because it is not clear whether the term encompasses sequences different from SEQ ID NO:1 or 3, or encompasses the exact sequence in claim limitation a.

Claims 1 and 2 recite the term "Seq ID NO 1 and/or 3" which is confusing because nucleic acids usually do not comprise both SEQ ID NO:1 and 3 which are separate AR42 and AR32 sequences.

Claim 1 recite "that corresponds to the sequence from a. within the scope of the degeneration of the genetic code" whose metes and bounds are not clear because an infinite number of correspondence can be made with the sequence and the term within the scope of the degeneration of the genetic code is not clear because the metes and bounds of what is "within scope" is unclear.

Claim 1 recite "hybridizes with the sequences from a. and/or b. under stringent conditions" whoses metes and bounds are not clear because the "stringent conditions" is a relative term. One skilled in the art hybridize under many conditions such as high and low which uses specific salt and temperature which can provide similar results and which conditions applies to the claims are not clear.

Claim 2 recite "it" which is indefinite because it is an indefinite pronoun and it is not clear what "it" is referring to.

Claim 3 recites the term "Seq ID NO 2 and/or 4" which is confusing because nucleic acids usually do not comprise both SEQ ID NO:2 and 4 which are separate AR42 and AR32 sequences.

Claim 13 recite "transfixed" whose metes and bounds are not clear because it is not a term that one of skilled in the art uses. One of skill in the art usually use the terms "transformed" or "transfected".

Claim 14 recite "selected from the group that consists of" which is not a proper Markush and encompasses all the cells simultaneously which is confusing. It is suggested that claims include proper Markush language.

Claim 15 provides for the use of a cell, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 2 recite recites the limitation "Nucleic acid" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 12 recite recites the limitation "a nucleic acid" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Claims 13 recite recites the limitation "a nucleic acid" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 13 recite recites the limitation "a vector" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claims 14 recite recites the limitation "Cell" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 15 recite recites the limitation "a cell" in line 1. There is insufficient antecedent basis for this limitation in the claim.

7. Claims 1-2 and 12-15 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

Claims 1-2 and 12-15 are drawn to a genus of DNAs which encode a genus of androgen receptors that are not defined by any critical or definitive structural limitations because of no structural limitation and the recitation of "hybridization" language. The specification only discloses a single species disclosed in Figure 1. Furthermore, page 18 of the specification teaches that androgen does not activate the AR42 or AR32 thus are not androgen receptor in the classical sense (Tilley et al., PNAS, 1989). The

specification does not disclose what structural features, other than the full length sequence of the AR42 or AR32, must be retained in order to render a protein as a androgen receptor. The specification fail to disclose what specific functions are considered to be definitive of androgen receptor and what specific structures are critical to their retention. The claims are drawn to a genus that need only be related or retain a function that is "characteristic" of a androgen receptor without a definition of what functions are characteristic and what structures other than the full length sequence of AR42 or AR32 are required for said functions. Without said information, the single species cannot be representative of such a broad genus. *University of California v. Eli Lilly and Co. (CAFC) 43 USPQ2d 1398* (*Eli Lilly*) held that a generic claim to human, mammalian or vertebrate protein when only the rat protein sequence was disclosed, did not have written description in the specification. The essential feature of the invention is the single species of DNA encoding the AR42 or AR32. The specification with a single species does not provide support for the claimed genus because *Eli Lilly* held that one skilled in the art could not envision the structure of the genus of proteins in other species such as human or the genus of mammalian or vertebrate proteins. In the same manner, one skilled in the art cannot envision the genus of andorgen receptors structure and thus the specification does not provide adequate disclosure for the claimed genus.

8. Claims 1-3 and 12-15 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the isolated nucleic acid encoding SEQ ID NO:2 or 4, the isolated vector comprising the above stated nucleic acid, isolated cell

comprising the the above stated isolated vector, and the method of expressing nucleic acid in the above stated host cell, does not reasonably provide enablement for the nucleic acid of claims 1-3, the vector of claim 12, the cells and methods of using the cell of claims 13-15. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The first paragraph of § 112 requires that the patent specification enable "those skilled in the art how to make and use the full scope of the claimed invention without `undue experimentation.'" Genentech, Inc. v. Novo Nordisk AIS, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)); see also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). ("[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art."). Whether making and using the invention would have required undue experimentation, and thus whether the disclosure is enabling is a legal conclusion based upon several underlying factual inquiries. See In re Wands, 858 F.2d 731, 735, 736-37, 8 USPQ2d 1400, 1402, 1404 (Fed. Cir. 1988). As set forth in Wands, the factors to be considered in determining whether a claimed invention is enabled throughout its scope without undue experimentation include the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the

prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

Likewise, in Amgen Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991), the court affirmed the holding of invalidity of claims to analogs of the EPO gene under § 112 for lack of enablement where applicants had claimed every possible analog of the EPO gene but had disclosed only how to make EPO and a very few analogs. "[D]espite extensive statements in the specification concerning all analogs of the EPO gene that can be made, there is little enabling disclosure of the particular analogs and how to make them .... There may be many other genetic sequences that code for EPO-type products. Amgen has told how to make and use only a few of them and is therefore not entitled to claim all of them." Id., 927 F.2d at 1213-14, 18 USPQ2d at 1027.

Claims 1-3 and 12-15 are too broad to be enabled by a specification that provides only AR42 and AR32 as examples of an embodiment of the claimed invention. Here, independent claims 1-3 are not limited to DNA encoding any specific androgen receptor from any particular species (e.g., mammal, amphibian, bird or fish). Furthermore, AR42 and AR32 are not androgen receptor in the classical sense that it binds androgen because the specification on page 18 teaches that it does not specifically activates with androgen receptor. While dependent claim 3 is limited to DNA encoding a SEQ ID NO:2 or 4, they are also not limited to any specific isotype or isoform because the claims encompass nucleic acid encoding both SEQ ID NO:2 and 4 simultaneously. The specification only describes one DNA sequence encoding AR42

and AR32 protein member from a large "gene family" from only one species, i.e., human. Claims 12-14 encompass vector or cells using the claims 1-3 which are not enabled for the same reason. Claim 15 encompass a possible method claims using the cells of claims 13-14 and are not enabled for the reasons set forth for claims 1-3.

The amount of direction provided in the specification is limited to isolation and characterization of AR42 and AR32 nucleic acid. The specification has identified a range of nucleotides and amino acid of AR42 and AR32, but not which nucleotides and amino acids are critical to binding a androgen ligand and a androgen receptor response element. Neither does the specification identify which amino acid and/or nucleic acid subsequences are conserved between many isotypes, or between species, e.g., mammals, fish, amphibians or birds. Thus, the specification provides no evidentiary basis for reasonably predicting how the primary sequence homology correlates to structural/functional homology. The specification does not teach the critical amino acid/nucleic acid sequences necessary to bind androgen and thereby unmasking the DBD of the receptor have not been identified. Even proteins with highly homologous sequences can function very differently for example 3-hemoglobin and its gene in normal individuals and patients with sickle cell anemia.

Furthermore, to the extent that the Southern blot/low stringency hybridization analysis described in the specification might suggest the existence of one or more genes encoding other proteins with closely related properties to AR42 or AR32, the specification does not describe the isolation and characterization of these genes or how to make them. Moreover, the fact that other androgen receptors have been isolated,

sequenced and characterized in subsequent publications does not lead to the conclusion that the specification taught how to make them. 24 Gould v. Quiaa, 822 F.2d 1074, 1078, 3 USPQ2d 1302, 1305 (Fed. Cir. 1987) ("A later dated publication cannot supplement an insufficient disclosure in a prior dated application to render it enabling.") Even the specification describes the hap gene identified by Dejean in 1986 and later identified as being the RAR gene, as giving an "unrelated" pattern under high stringency hybridization analysis.

Assuming arquendo that other DNA sequences were isolated by a low stringency hybridization analysis as described in the specification, whether those DNAs actually encoded androgen receptors or encoded receptors for other ligands appears unpredictable, i.e., a ligand screening assay based on chimeric receptor constructs would have to be performed which would require undue experimentation. As to the state of the art, the modular nature or "domain" organization of nuclear receptor proteins "was first noted in a sequence alignment of the androgen receptors of different species" by Tilley et al. (PNAS 1989). Thus, the state of the art appears to be evolving, rather than mature.

Claims 13-15 encompass cells or method of using cells where the cells are transfixed with nucleic acid of claims 1-3 which are not in vector forms. One skilled in the art do not transform or transfect cells with nucleic acid which are not packaged in the vectors (Tilley et al., PNAS, 1989). It would require undue experimentation to transform or transfect cells without a vector because there is no selection to maintain the nucleic acid in the cells.

Therefore, based on the above Wands analysis, a preponderance of the evidence supports a conclusion that one skilled in the art would not have been enabled to make and use the invention of claims without undue experimentation.

Priority

9. Applicant's claim for domestic priority under 35 U.S.C. 120 is acknowledged. However, the applications upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 1-3 and 12-15 of this application for the reasons provided above. See MPEP 706.02.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1-2 and 12-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Zamecnik et al. (WO 97/11170).

Zamecnik et al. disclose a nucleic acid encoding a protein (pages 22-28) which is 98% identical to claimed SEQ ID NO: 2 and vectors, cells comprising the DNA and methods of expressing the DNA (pages 14-15).

10. Claims 1-3 and 12-15 are rejected under 35 U.S.C. 102(e) as being anticipated by Kausch et al. (US 5,508,164)

Kausch et al. disclose the isolation of chromosome (column 5). The cell source are human cells (column 6, lines 5-15). Many chromosomes can be sorted at once (column 9, lines 29-43). Large amounts of pure chromosomes and DNA of the chromosomes is isolated (column 10, lines 22-25). Cells transfected with chromosomal DNA is disclosed (column 10, lines 22-25).

Claims encompass chromosomal DNA because the claims encompass polynucleotide sequence comprising the polynucleotide sequence encoding a

polypeptide with SEQ ID NO:2 or 4 which encompasses the genomic DNA. The claims drawn generically to hybridization is met by the genomic DNA of Kaush et al. The isolated and purified chromosomes comprise the polynucleotide sequence encoding a polypeptide with SEQ ID NO:2 or 4. Chromosomal DNA inherently are operably linked to an expression control sequences. Chromosomal DNA inherently comprises heterologous sequence because it undergoes recombination.

11. No claim is allowed.

12. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Pak, whose telephone number is (571) 272-0879. The examiner can normally be reached on Monday through Friday from 8:30 AM to 2:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (571) 272-0829.

The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306. Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael D. Pak

Michael Pak
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Art Unit 1646
14 Ocotober 2005